

What is claimed:

1 1. A method of assessing a candidate molecule for the treatment of a CNS disorder, said method
2 comprising:

- a) providing a test DAO-inhibitor or DDO-inhibitor compound; and
- b) administering said compound to an animal model of schizophrenia or bipolar disorder,

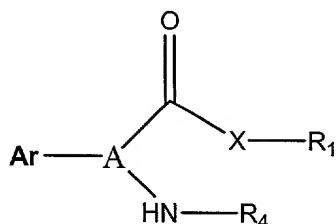
wherein a determination that said compound ameliorates a characteristic representative of a CNS disorder in said animal model indicates that said compound is a candidate molecule for the treatment of a CNS disorder; and alternatively one or more of the following:

- i.) wherein said compound selectively bind to said polypeptide;
- ii.) wherein said compound selectively inhibits the activity of said polypeptide;
- iii.) wherein said compound is capable of inhibiting the oxidation or degradation of a D-amino acid selected from the group consisting of D-Met, D-Pro, D-Phe, D-Tyr, D-Ile, D-Leu, D-Ala, D-Val, D-Ser, D-Arg, D-His, D-norleucine, D-Trp, D-Ornithine, cis-4-hydroxy-D-proline, D-Thr, D-Trp-methyl ester, N-acetyl-D-Ala, D-Lys, D-Asp, D-Glu, D-Asn, D-Gln, D-Asp-dimethyl-ester and N-methyl-D-Asp; and further alternatively wherein the compound of claim iii is capable of inhibiting the oxidation or degradation of D-serine.

20

1 2. The method of claim 1, wherein said test compound is selected from the group consisting
2 of:

3 (1) a compound represented by the structure comprising:



5 or a pharmaceutically acceptable salt thereof, wherein:

6 a) A is alkyl such as methyl, ethyl, propyl or butyl; branched chain alkyl such as
7 isobutyl, isopropyl, isopentyl or cycloalkyl such as cyclopropyl, cyclopentyl or
8 cyclohexyl. Such groups may themselves be substituted with C₁-C₆ alkyl, halo,
9 hydroxyl or amino;

10 b) X is O or N;

11 c) Ar is an aromatic mono-, bi- or tricyclic fused heterocyclic ring, wherein the ring is
12 either unsubstituted or substituted in one to five position(s) with hydrogen, halogen,
13 hydroxyl, -CN, COR₂, --CONR₂R₃, --S(O)_nR₂, --OPO(OR₂)OR₃, --PO(OR₃)R₃, --
14 OC(O)NR₂R₃, --COOR₂, --CONR₂R₃, --SO₃H, --NR₂R₃, --NR₂COR₃, --NR₃
15 COOR₃, --SO₂NR₂R₃, --N(R₂)SO₂R₃, --NR₂CONR₂R₂, --SO₂NHCOR₂, --
16 CONHSO₂R₂, --SO₂NHCN, --OR₁, C₁-C₆ straight or branched chain alkyl or
17 alkenyl, or C₁-C₆ branched or straight chain alkyl or alkenyl which is substituted
18 with one or more, halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro,
19 alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, Ar¹, N₃ or a
20 combination thereof and wherein the heterocyclic ring contains 1-6 heteroatom(s)
21 selected from the group consisting of O, N, S, and a combination thereof;

22 d) R₄ is H, alkyl, Ar¹, O, substituted alkyl;

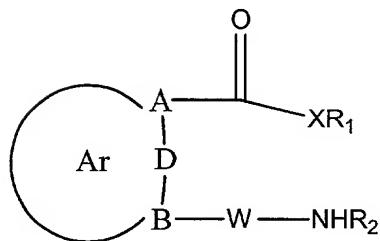
23 e) R¹ is (C₁ - C₆) alkyl, Ar¹, (C₁ - C₄) alkoxy carbonylmethyl, substituted alkyl;

24 f) R₂ and R₃ are each, independently, hydrogen, C₁-C₆ straight or branched chain alkyl
25 or alkenyl, or C₁-C₆ branched or straight chain alkyl or alkenyl which is substituted
26 with one or more, halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro,
27 alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, Ar¹, or N₃; and

28 g) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either
29 unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro,
30 trifluoromethyl, C₁ - C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁
31 -C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the
32 individual ring sizes are 3-7 members; and wherein the heterocyclic ring contains 1-
33 6 heteroatom(s) selected from the group consisting of O, N, S, and a combination
34 thereof;

35

36 (2) a compound represented by the structure comprising:



37

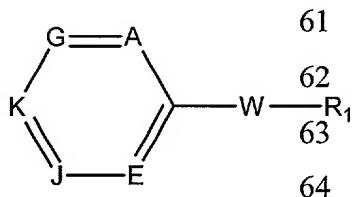
38 wherein:

- 39 a) A and B consist of C or N and D may contain 0-2 members consisting of C or N;
- 40 b) W is C₁-C₄ alkyl such as (CH₂)_n, branched chain alkyl;
- 41 c) n is 0-4. Further, when n = 0 it is assumed that -NHR₂ is covalently bound to B;
- 42 d) X is O or N;
- 43 e) R₂ is H, alkyl, Ar¹, or O substituted alkyl;
- 44 f) R¹ is (C₁ - C₆) alkyl, Ar¹, (C₁ - C₄) alkoxy carbonylmethyl, or substituted alkyl;
- 45 g) Ar is an aromatic mono-, bi- or tricyclic fused heterocyclic ring, wherein the ring is
46 either unsubstituted or substituted in one to six position(s) with halo, hydroxyl,
47 nitro, trifluoromethyl, C₁ - C₆ straight or branched chain alkyl or alkenyl, C₁-C₄
48 alkoxy, C₁ - C₄ alkenyloxy, phenoxy, benzyloxy, amino, C₃-C₆ cycloalkyl or a
49 combination thereof; wherein the individual ring sizes are 5-6 members; and
50 wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group
51 consisting of O, N, S, and a combination thereof; and
- 52 h) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either
53 unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro,
54 trifluoromethyl, C₁ - C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁
55 -C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the
56 individual ring sizes are 3-7 members; and wherein the heterocyclic ring contains 1-
57 6 heteroatom(s) selected from the group consisting of O, N, S, and a combination
58 thereof; and

59

59 (3) a compound represented by the structure comprising:

60

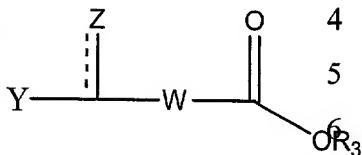


65 wherein:

- 66 a) A, G, K, J, E are members of a six membered carbo or heterocyclic aromatic ring,
67 wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group
68 consisting of C, N and a combination thereof;
- 69 b) A, G, K, J, E may each independently be unsubstituted or substituted with hydrogen,
70 halogen, hydroxyl, -CN, COR₂, --CONR₂R₃, --S(O)_nR₂, --OPO(OR₂)OR₃, --
71 PO(OR₃)R₃, --OC(O)NR₂R₃, --COOR₂, --CONR₂R₃, --SO₃H, --NR₂R₃, --NR₂
72 COR₃, --NR₃COOR₃, --SO₂NR₂R₃, --N(R₂)SO₂R₃, --NR₂CONR₂R₂, --SO₂
73 NHCOR₂, --CONHSO₂R₂, --SO₂NHCN, --OR₁, C₁-C₆ straight or branched chain
74 alkyl or alkenyl, or C₁-C₆ branched or straight chain alkyl or alkenyl which is
75 substituted with one or more halogen, hydroxyl, amino, carboxy, carboxamide,
76 nitrile, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, Ar¹,
77 or N₃;
- 78 c) R₁ is CN, COR₂, --CONR₂R₃, --S(O)_nR₂, --OPO(OR₂)OR₃, --PO(OR₃)R₃, --
79 OC(O)NR₂R₃, --COOR₂, --CONR₂R₃, --SO₃H, --NR₂R₃, --NR₂COR₃, --NR₃
80 COOR₃, --SO₂NR₂R₃, --N(R₂)SO₂R₃, --NR₂CONR₂R₂, --SO₂NHCOR₂, --
81 CONHSO₂R₂, --SO₂NHCN, SCN, COCO₂H, C₁-C₆ straight or branched chain
82 alkyl or alkenyl, or C₁-C₆ branched or straight chain alkyl or alkenyl which is
83 substituted with one or more halogen, hydroxyl, amino, carboxy, carboxamide,
84 nitrile, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, Ar¹,
85 or N₃;
- 86 d) W is N, (CH₂)_x, or -NCH₂;
- 87 e) x=0-4;
- 88 f) n=0-2;

89 g) R₂ and R₃ are each, independently, hydrogen, C₁-C₆ straight or branched chain alkyl
 90 or alkenyl, or C₁-C₆ branched or straight chain alkyl or alkenyl which is substituted
 91 with one or more halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro,
 92 alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, Ar¹, or N₃; and
 93 h) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either
 94 unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro,
 95 trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁
 96 -C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the
 97 individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-
 98 6 heteroatom(s) selected from the group consisting of O, N, S, and a combination
 99 thereof.

1 3. The method of claim 1, wherein said test compound is selected from the group consisting of
 2 (1) a compound represented by the structure comprising:

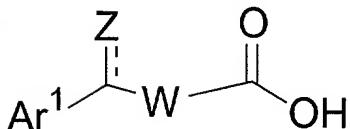


7 wherein:

8 a) W=(CH₂)_n ;
 9 b) n=0-5;
 10 c) Z is O or hydroxyl;
 11 d) Y=H, Ar¹, R₁(CH₂)_x, R₁S(CH₂)_x--, R₁SO(CH₂)_x--, R₁SO₂(CH₂)_x--, R₁SO₃(CH₂)_x--,
 12 HNR₁SO₂(CH₂)_x--, R₁R₂N(CH₂)_x, R₁O(CH₂)--, CF₃, or OH;
 13 e) x=0-6;
 14 f) R₁, R₂ and R₃ are each independently hydrogen, C₁-C₆ straight or branched chain
 15 alkyl or C₁-C₆ branched or straight chain alkyl substituted with one or more
 16 halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro, alkoxy,
 17 trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, or Ar¹;

18 g) R₄ is halogen, CN, N₃, C₁-C₆ straight or branched chain alkyl or C₁-C₆ branched or
 19 straight chain alkyl substituted with one or more halogen, hydroxyl, nitro, alkoxy,
 20 trifluoromethyl, sulfonate, phosphonate, phosphate, Ar¹, --COR₁, --COOR₁, --
 21 CONR₁R₂, CN, --NR₁, --NR₁R₂, --SR₁, --SO₂NHCN, or N₃; and
 22 h) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either
 23 unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro,
 24 trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁
 25 -C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the
 26 individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-
 27 6 heteroatom(s) selected from the group consisting of O, N, S, and a combination
 28 thereof; and

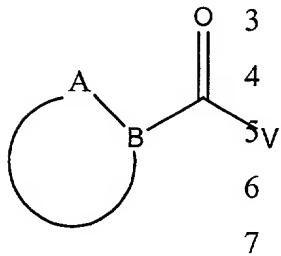
29
 30 (2) a compound represented by the structure comprising:



31 wherein:

32
 33 a) Y is Ar¹;
 34 b) Z is a carbonyl or hydroxyl;
 35 c) W is (CH₂)_n wherein (n= 0,1, or 2) and R₃ = H; and
 36 d) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either
 37 unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro,
 38 trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁
 39 -C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the
 40 individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-
 41 6 heteroatom(s) selected from the group consisting of O, N, S, and a combination
 42 thereof.

1 4. The method of claim 1, wherein said test compound is represented by the structure
 2 comprising:

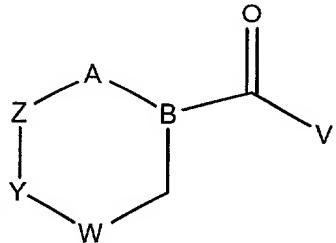


8 wherein:

- 9 a) A and B taken together, form a 5-8 membered saturated or partially unsaturated
 10 heterocyclic ring containing at least one additional O, S, SO, SO₂, NH, or NR¹
 11 heteroatom in any chemically stable oxidation state;
- 12 b) V is O, OR₁, NR₂, NR₁R₂, CHR₁R₂, CH₂R₃, CHR₃R₄, or CH₂N₃;
- 13 c) R₁ and R₂ are independently hydrogen, C₁-C₆ straight or branched chain alkyl or C₁-
 14 C₆ branched or straight chain alkyl substituted with one or more halogen, hydroxyl,
 15 amino, carboxy, carboxamide, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate,
 16 phosphonate, or Ar¹;
- 17 d) R₃ and R₄ are either halogen, C₁-C₆ straight or branched chain alkyl or C₁-C₆
 18 branched or straight chain alkyl substituted with one or more hydroxyl, amino,
 19 carboxy, carboxamide, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate,
 20 phosphonate, Ar¹, --OC(O)R₁, --COOR₁, --CONR₁R₂, CN, NR₁, NR₁R₂, SR₁,
 21 SO₂NHCN, or N₃; and
- 22 e) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either
 23 unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro,
 24 trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-
 25 -C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the
 26 individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-
 27 6 heteroatom(s) selected from the group consisting of O, N, S, and a combination
 28 thereof.

1 5. The method of claim 4, wherein said compound is cystathionine ketimine or cyclothionine

1 6. The method of claim 1, wherein said test compound is represented by the structure
2 comprising:



3 wherein:

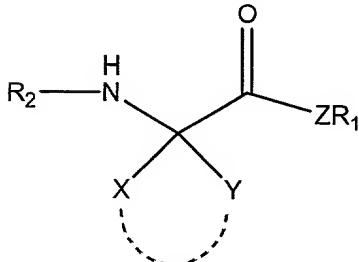
- 4 a) W-Y-Z-A-B comprise a six membered saturated or partially saturated carbocyclic or
5 heterocyclic ring, wherein the heterocyclic ring contains heteroatom(s) selected from
6 the group consisting of O, N, S, and any combination thereof;
- 7 b) B is either C, CH or N;
- 8 c) A, W, Y, Z are each independently CH₂, CHR₃, CR₃R₄, O, S, SO, SO₂, NH, NR₁,
9 NR₁R₂, or C=O;
- 10 d) V is O, OR₁, NR₂, NR₁R₂, CHR₁R₂, CH₂R₃, CHR₃R₃, or CH₂N₃;
- 11 e) R₁ and R₂ are independently hydrogen, C₁-C₆ straight or branched chain alkyl or C₁-
12 C₆ branched or straight chain alkyl substituted with one or more, halogen, hydroxyl,
13 amino, carboxy, carboxamide, nitrile, nitro, alkoxy, trifluoromethyl, sulfur,
14 sulfonate, phosphonate, phosphate, or Ar¹;
- 15 f) R₃ and R₄ are each independently halogen, --OC(O)R₁, --COOR₁, --CONR₁R₂, CN,
16 --NR₁, --NR₁R₂, --SR₁, --SO₂NHCN, N₃, C₁-C₆ straight or branched chain alkyl or
17 C₁-C₆ branched or straight chain alkyl substituted with one or more halogen,
18 hydroxyl, nitro, alkoxy, trifluoromethyl, sulfonate, phosphonate, Ar¹, --OC(O)R₁, --
19 COOR₁, --CONR₁R₂, CN, --NR₁, --NR₁R₂, --SR₁, --SO₂NHCN, or N₃; and
- 20 g) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either
21 unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro,
22 trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-
23 C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the

25 individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-
 26 6 heteroatom(s) selected from the group consisting of O, N, S, and any combination
 27 thereof.

1 7. The method of claim 6, wherein said compound is selected from the group consisting of:
 2 Aminoethylcysteine-ketimine (2H-1,4-thiazine-5,6-dihydro-3-carboxylic acid), Thiomorpholine-2-
 3 carboxylic acid, Lanthionine ketimine, and 1,4-Thiomorpholine-3,5-dicarboxylic acid.

1 8. The method of claim 1, wherein said test compound is selected from the group consisting
 2 of:

3 (1) a compound represented by the structure comprising:

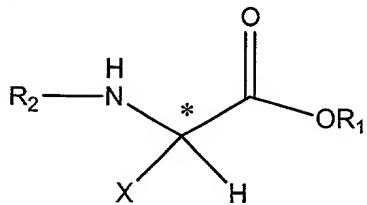


5 wherein:

- 6 a) Z is O or NH;
- 7 b) R¹ is (C₁-C₆) alkyl, Ar¹, or (C₁-C₄) alkoxy carbonylmethyl;
- 8 c) X, Y, independently of one another, are H, Ar¹, (C₁-C₆) alkyl (which can be
 9 interrupted or substituted by heteroatoms, such as N, P, O, S or Si, it being possible
 10 for the heteroatoms themselves to be substituted by (C₁-C₃) alkyl once or several
 11 times), (C₂-C₆) alkenyl, (C₁-C₆) haloalkyl, or halogen. When X and Y are each
 12 carbon they may be covalently joined to form a saturated or partially unsaturated
 13 carbocyclic compound of 3-8 members consisting independently of C, N, O, and S,
 14 further wherein ring members may themselves be unsubstituted or substituted with
 15 halo, hydroxyl, carboxy, nitro, trifluoromethyl, C₁-C₆ straight or branched chain

16 alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino,
 17 substituted alkyl, Ar¹, or a combination thereof;
 18 d) R₂ is H, alkyl, Ar¹, or O substituted alkyl; and
 19 e) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either
 20 unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro,
 21 trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁
 22 -C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the
 23 individual ring sizes are 3-7 members; and wherein the heterocyclic ring contains 1-
 24 6 heteroatom(s) selected from the group consisting of O, N, S, and any combination
 25 thereof;

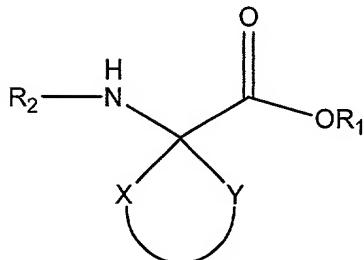
26 (2) a compound represented by the structure comprising:



27 wherein:

28 a) * = asymmetric center and
 29 b) R¹ = (C₁ - C₆) alkyl, Ar¹, (C₁ - C₄) alkoxy carbonylmethyl and
 30 c) X is H, (C₁ - C₆) alkyl (which can be interrupted or substituted by heteroatoms, such
 31 as N, P, O, S or Si, it being possible for the heteroatoms themselves to be substituted
 32 by (C₁ - C₃) alkyl once or several times), (C₂-C₆) alkenyl, (C₁ - C₆) haloalkyl,
 33 halogen, or Ar¹;
 34 d) R₂ is H, alkyl, Ar¹, or O substituted alkyl;
 35 e) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either
 36 unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro,
 37 trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁
 38 -C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the
 39 individual ring sizes are 3-7 members; and wherein the heterocyclic ring contains 1-
 40 6 heteroatom(s) selected from the group consisting of O, N, S, and any combination
 41 thereof;

43 (3) a compound represented by the structure comprising:

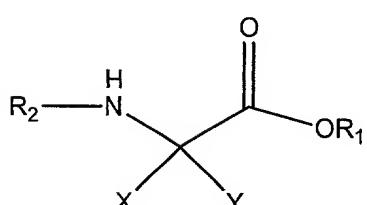


44

45 wherein:

- 46 a) X and Y are each carbon;
- 47 b) X and Y are connected by a saturated or partially saturated ring of 3-8 carbons and
48 such a ring may itself be substituted in one to five position(s) with halo, hydroxyl,
49 carboxy, amino, nitro, cyano, trifluoromethyl, C_1 - C_6 straight or branched chain alkyl
50 or alkenyl, C_1 - C_4 alkoxy, C_1 - C_4 alkenyloxy, or substituted alkyl groups;
- 51 c) R^1 is (C_1 - C_6) alkyl, Ar^1 , or (C_1 - C_4) alkoxy carbonylmethyl;
- 52 d) R_2 is H , alkyl, Ar^1 , or O substituted alkyl; and
- 53 e) Ar^1 is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either
54 unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro,
55 trifluoromethyl, C_1 - C_6 straight or branched chain alkyl or alkenyl, C_1 - C_4 alkoxy, C_1
56 - C_4 alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the
57 individual ring sizes are 3-7 members; and wherein the heterocyclic ring contains 1-
58 6 heteroatom(s) selected from the group consisting of O, N, S, and any combination
59 thereof; and

60 (4) a compound represented by the structure comprising:



61

62 wherein:

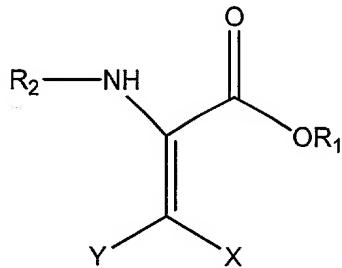
- 63 a) X , Y , independently of one another, are H , Ar^1 , (C_1 - C_6) alkyl (which can be
64 interrupted or substituted by heteroatoms, such as N, P, O, S or Si, it being possible

for the heteroatoms themselves to be substituted by (C₁-C₃) alkyl once or several times), (C₂-C₆) alkenyl, (C₁-C₆) haloalkyl, or halogen such as naphthyl or phenyl;

b) R₂ is H, alkyl, Ar¹, or O substituted alkyl; and

c) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 3-7 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and any combination thereof.

9. The method of claim 1, wherein said test compound is represented by the structure comprising:



wherein:

a) R¹ is (C₁-C₆) alkyl, Ar¹, or (C₁-C₄) alkoxy carbonylmethyl;

b) R₂ is H, alkyl, Ar¹, or O substituted alkyl;

c) Y is H, Ar¹, (C₁-C₆) alkyl (which can be interrupted or substituted by heteroatoms, such as N, P, O, S or Si, it being possible for the heteroatoms themselves to be substituted by (C₁-C₃) alkyl once or several times), (C₂-C₆) alkenyl, (C₁-C₆) haloalkyl, or halogen; and

d) X is alkyl or phenyl.

1 10. A method of diagnosing, detecting a predisposition to or susceptibility to schizophrenia,
2 depression or bipolar disorder in a subject, comprising
3 (a) obtaining a nucleic acid sample from said subject; and
4 (b) determining the identity of a nucleotide at a DAO-related polymorphism, or the
5 complement thereof in said biological sample.

1 11. A isolated or purified nucleic acid encoding a DAO polypeptide or DAO polypeptide
2 selected from the group consisting of:
3 (i) a nucleic acid molecule encoding a polypeptide comprising an amino acid sequence
4 selected from the group of sequences consisting of SEQ ID NOS 8 to 10; and
5 (ii) a nucleic acid molecule comprising a nucleic acid sequence selected from the group
6 of sequences consisting of SEQ ID NOS 1 to 6, or a sequence complementary
7 thereto;
8 (iii) a purified or isolated DAO polypeptide comprising an amino acid sequence selected
9 from the group of sequences consisting of SEQ ID NOS 8 to 10.
10 (iv) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid
11 sequence selected from the group of sequences consisting of SEQ ID NOS 1 to 6, or
12 a sequence complementary thereto.

1 12. The method of claim 1, wherein said test compound (i) binds to a DAO or DDO
2 polypeptide, or (ii) inhibits the activity of a DAO or DDO polypeptide.

1 13. A method of identifying a candidate molecule for the treatment of a CNS disorder, said
2 method comprising:

3 (a) contacting a DAO or DDO polypeptide or a biologically active fragment thereof
4 with a test compound;

5 (b) determining whether said compound (i) binds to said polypeptide, or (ii) inhibits the
6 activity of said polypeptide; and

7 (c) if said compound binds to said polypeptide or inhibits said polypeptide,
8 administering said compound to an animal model of schizophrenia, depression or
9 bipolar disorder,

10 wherein a determination that said compound ameliorates a characteristic representative of CNS
11 disorder in said animal model indicates that said compound is a candidate molecule for the
12 treatment of a CNS disorder.